Advantages & Disadvantages of Drug Testing in Alternative Matrices

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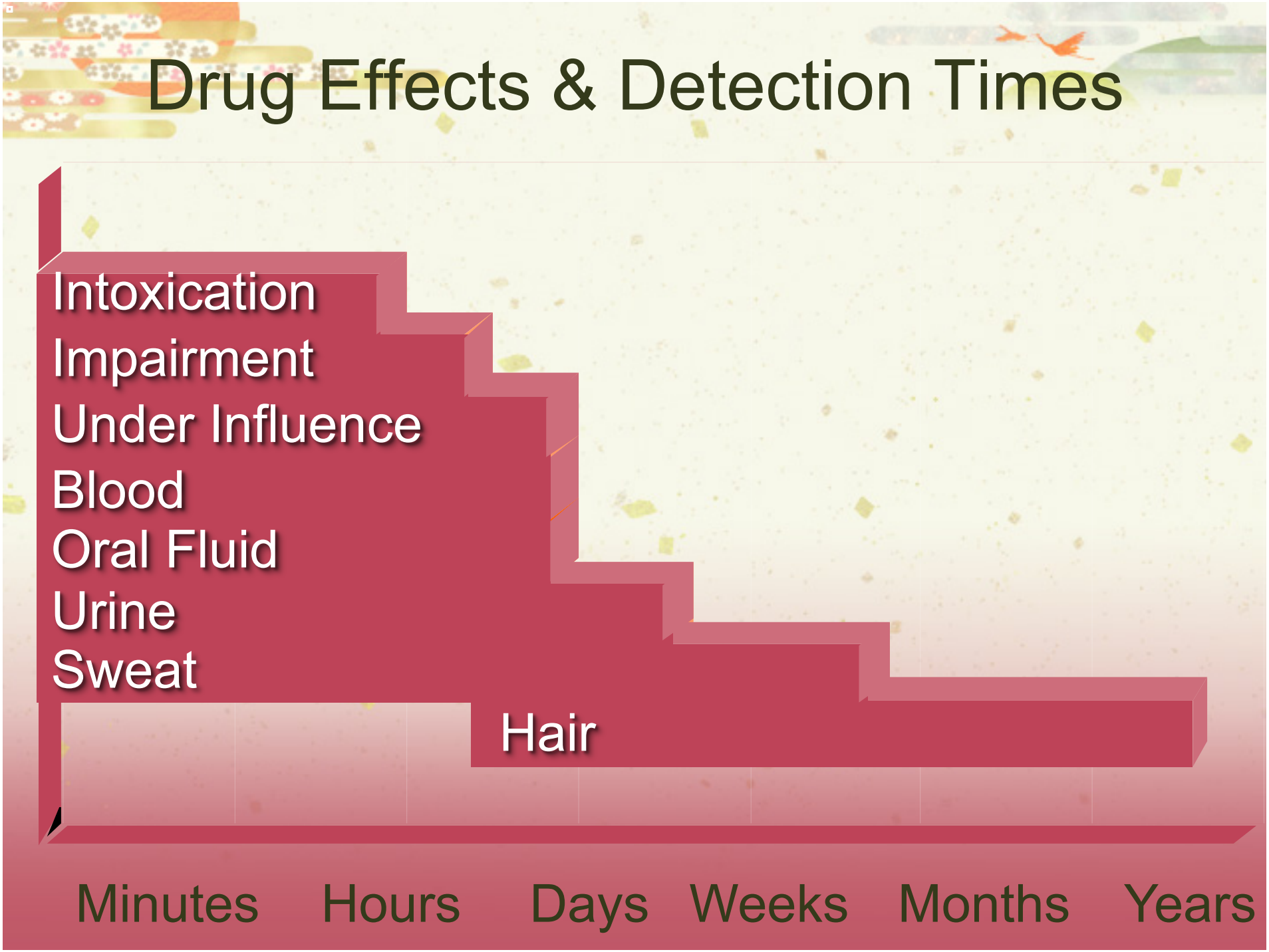
NIDA NATIONAL INSTITUTE ON DRUG ABUSE

Chemistry & Drug Metabolism

- Employ chemical & toxicological tools to address human drug abuse
- Our clinical research focuses on behavioral & physiological toxicities of drug use
- Identify & quantify biomarkers of drug use in complex biological matrices
- Correlate with drug's pharmacodynamic effects
- Provide framework for understanding mechanisms of drug action & toxicity, & for interpreting drug test results in individuals

Drug Effects & Detection Times



Urine Drug Testing

- Advantages
  - Sufficient specimen volume
  - Known testing accuracy/reliability
  - Known analytes & cutoffs to measure
  - Extensive clinical studies inform interpretation of results
  - Choice of on-site technologies for rapid results
  - Easily automated
  - Less expensive

Urine Drug Testing

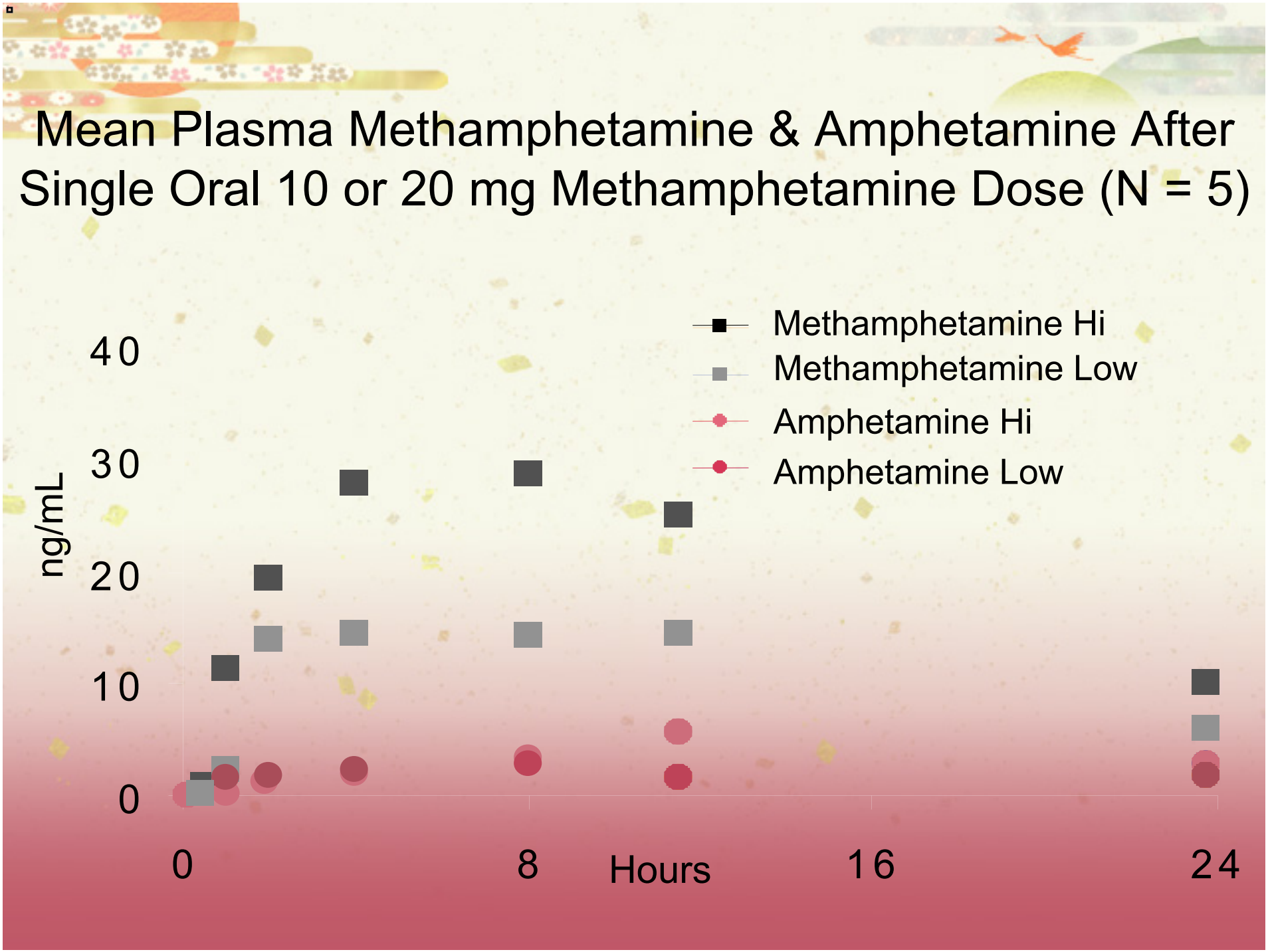
- Disadvantages
  - Collection difficult
    - Same gender collection
    - Considered invasion of privacy
    - Donors may be unable to provide specimen (Shy bladder)
  - Ease of adulteration & dilution with chemicals or simply excess water
  - Measure of exposure only
  - Not correlated with pharmacodynamic effects
  - Difficult to differentiate new drug exposure from residual drug excretion

Potential Advantages of Alternate Matrices

- Unique information
- Less invasive collection
- Multiple sampling
- Parent drug
- Greater stability
- Lower disease risk
- Longer detection window for some
- Easier collection, shipment & storage

Oral Fluid (Saliva)

Mean Plasma Methamphetamine & Amphetamine After Single Oral 10 or 20 mg Methamphetamine Dose (N = 5)



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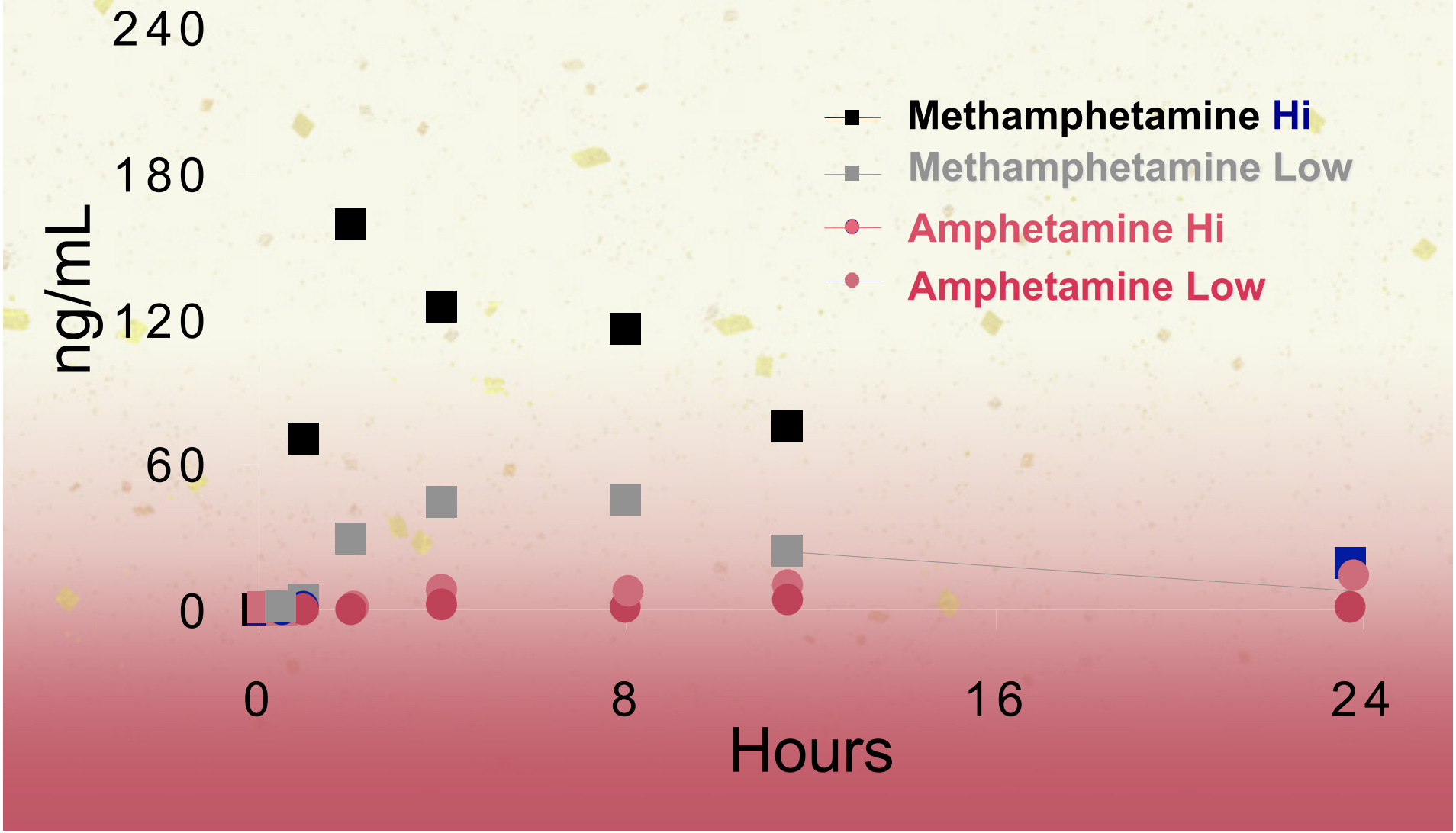
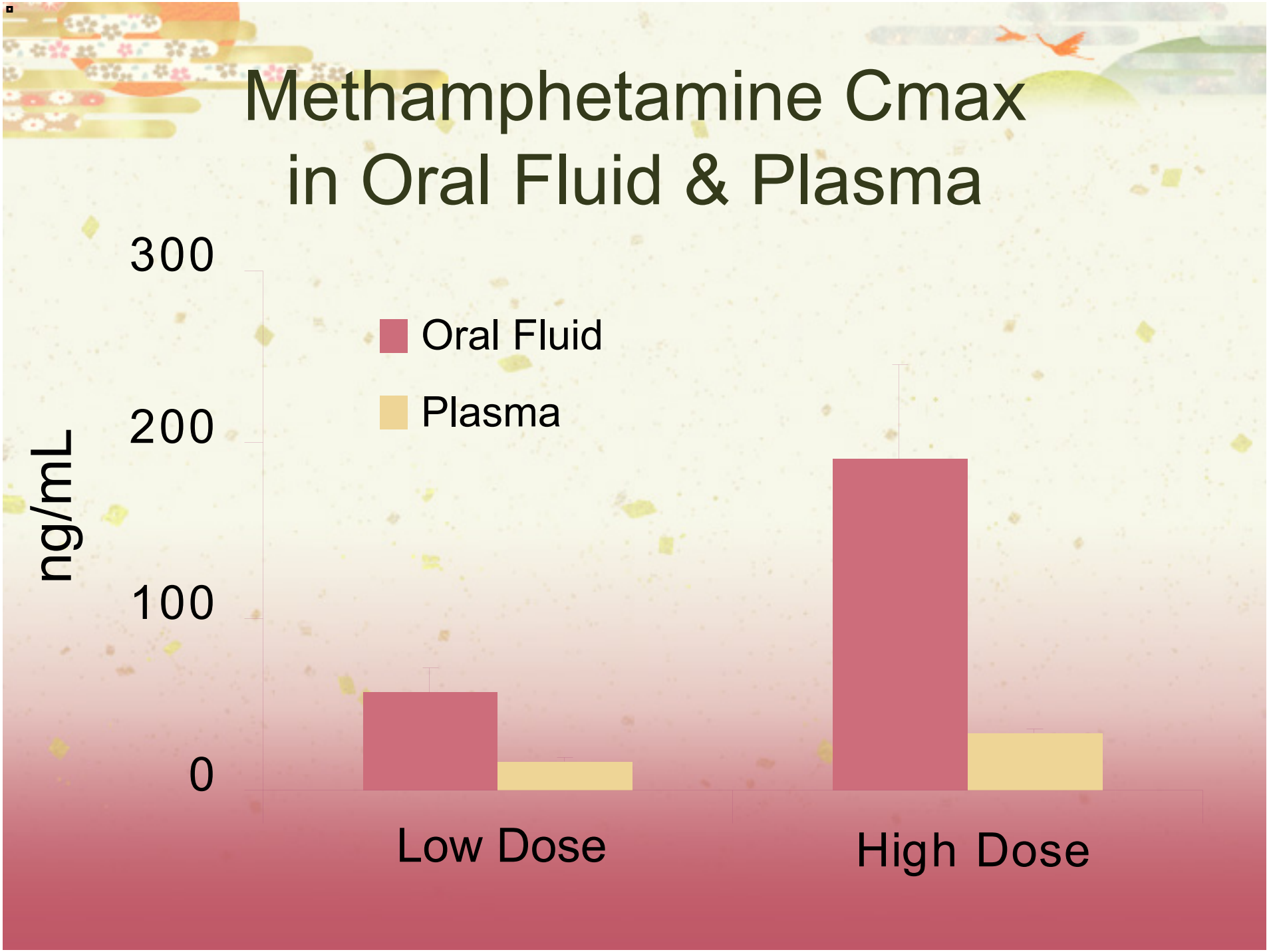
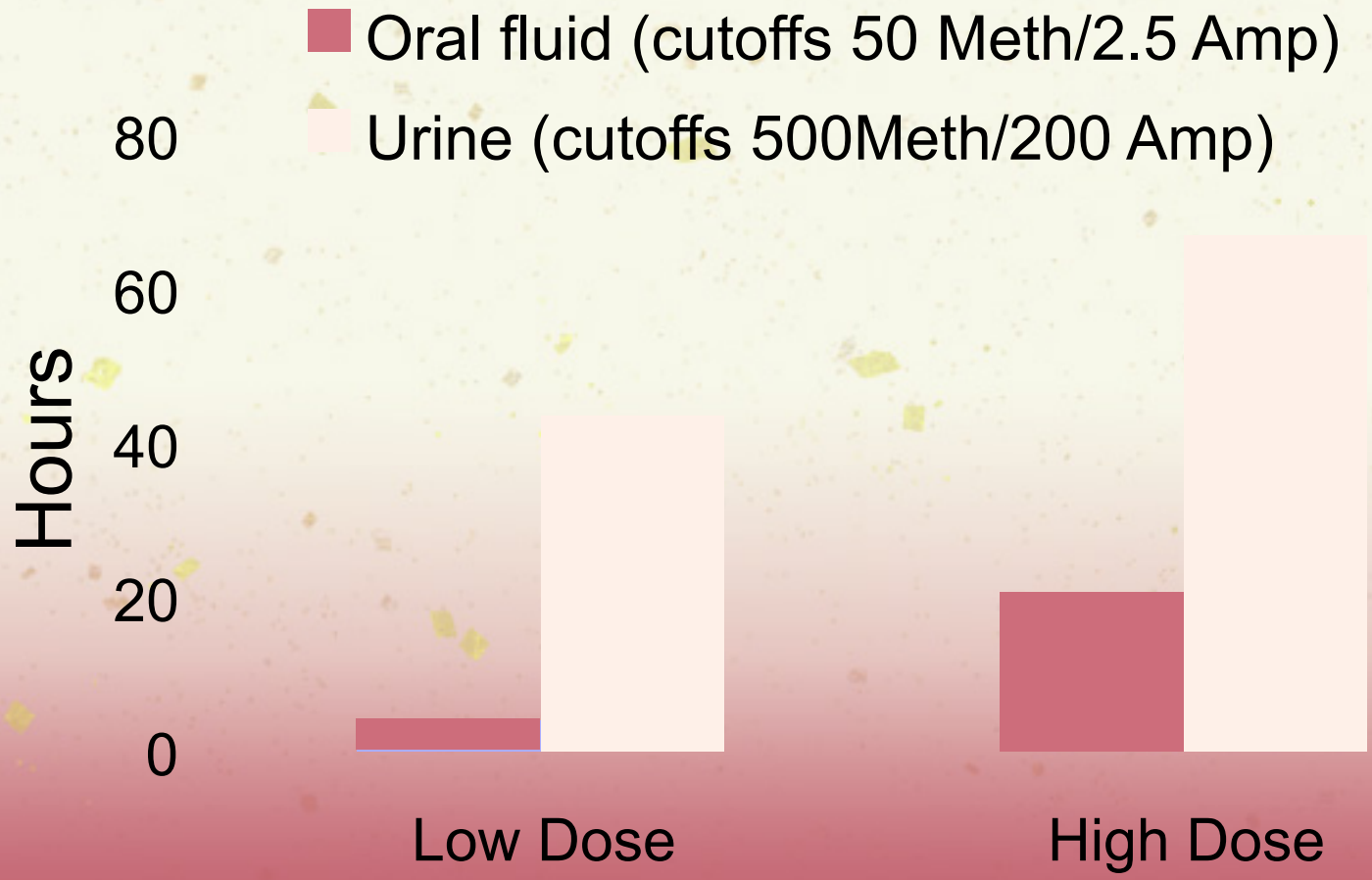


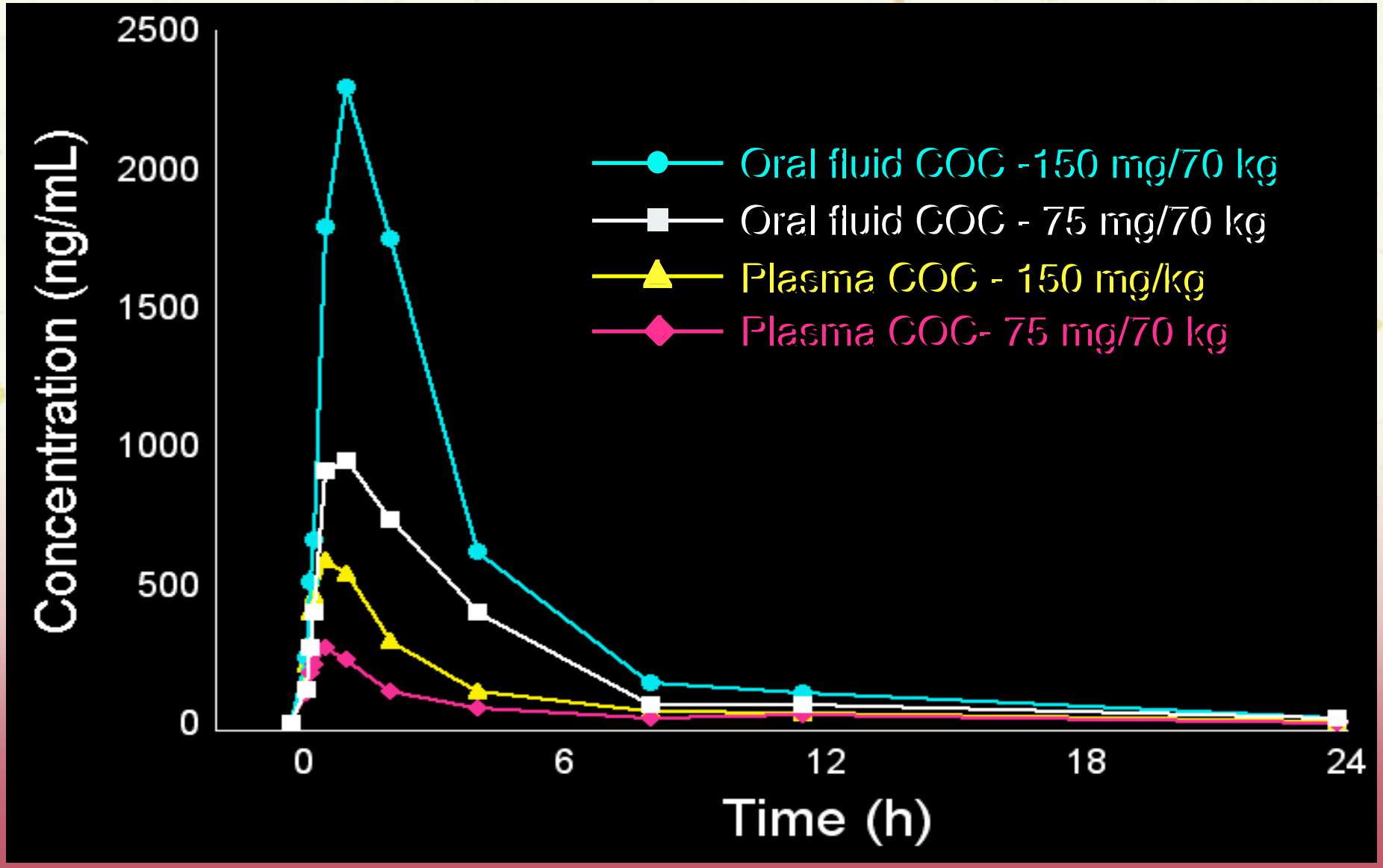
Methamphetamine Cmax in Oral Fluid & Plasma



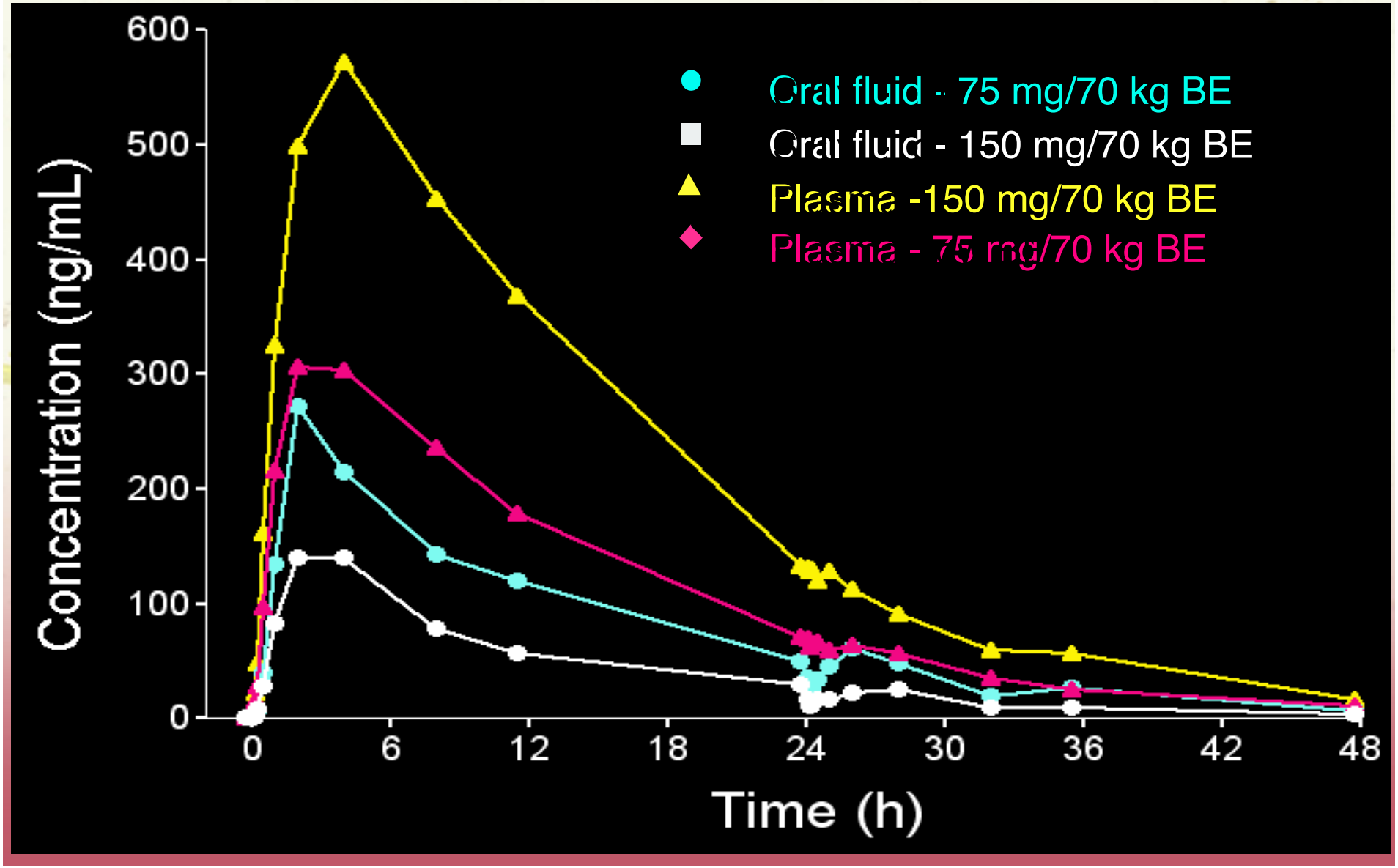
Methamphetamine Detection Times in Oral Fluid & Urine After 10 & 20 mg MAMP



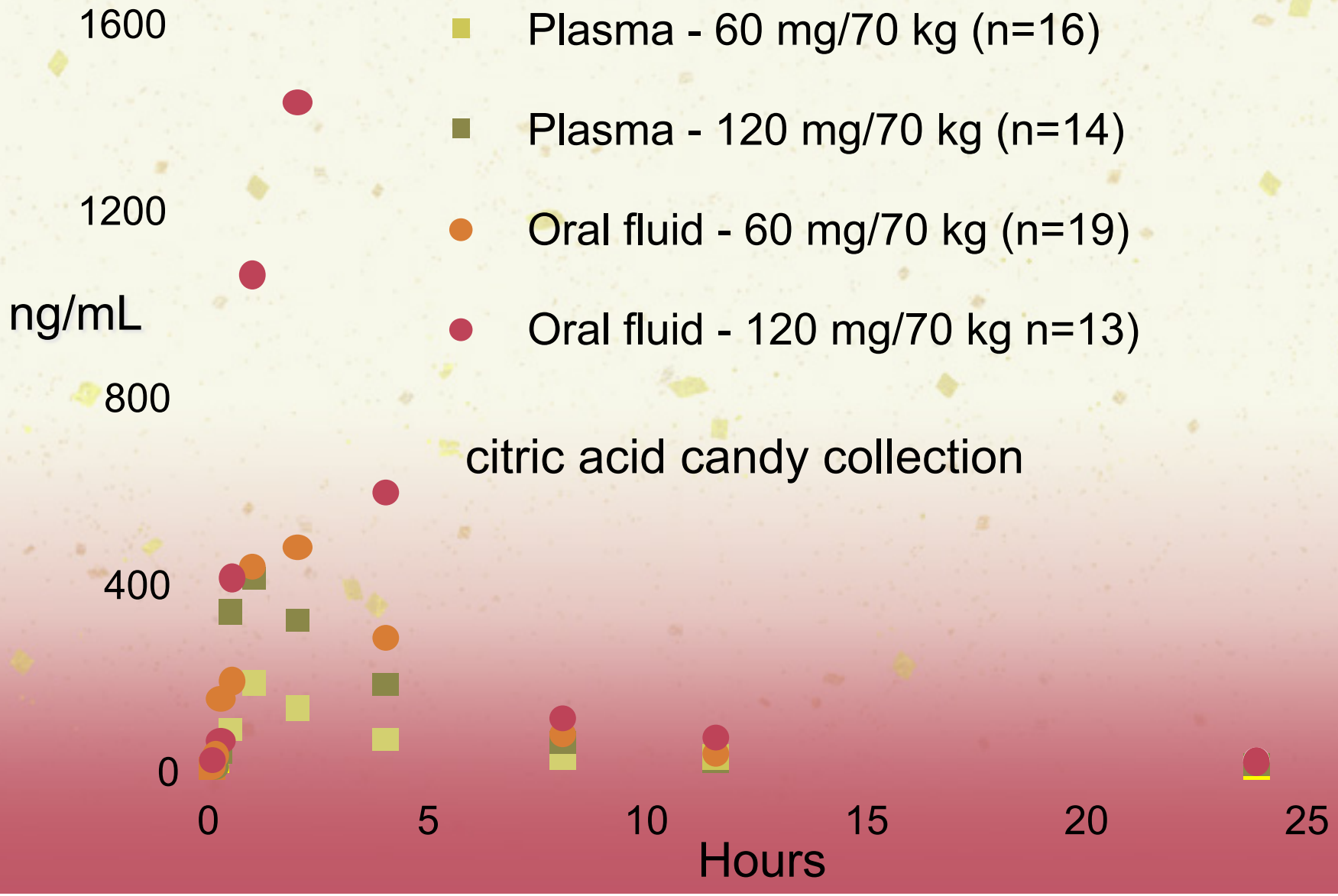
Cocaine


Concentration (ng/mL)
2500
2000
1500
1000
500
0
0
6
12
18
24
Time (h)
Oral fluid COC -150 mg/70 kg
Oral fluid COC - 75 mg/70 kg
Plasma COC - 150 mg/kg
Plasma COC- 75 mg/70 kg

Benzoylecgonine



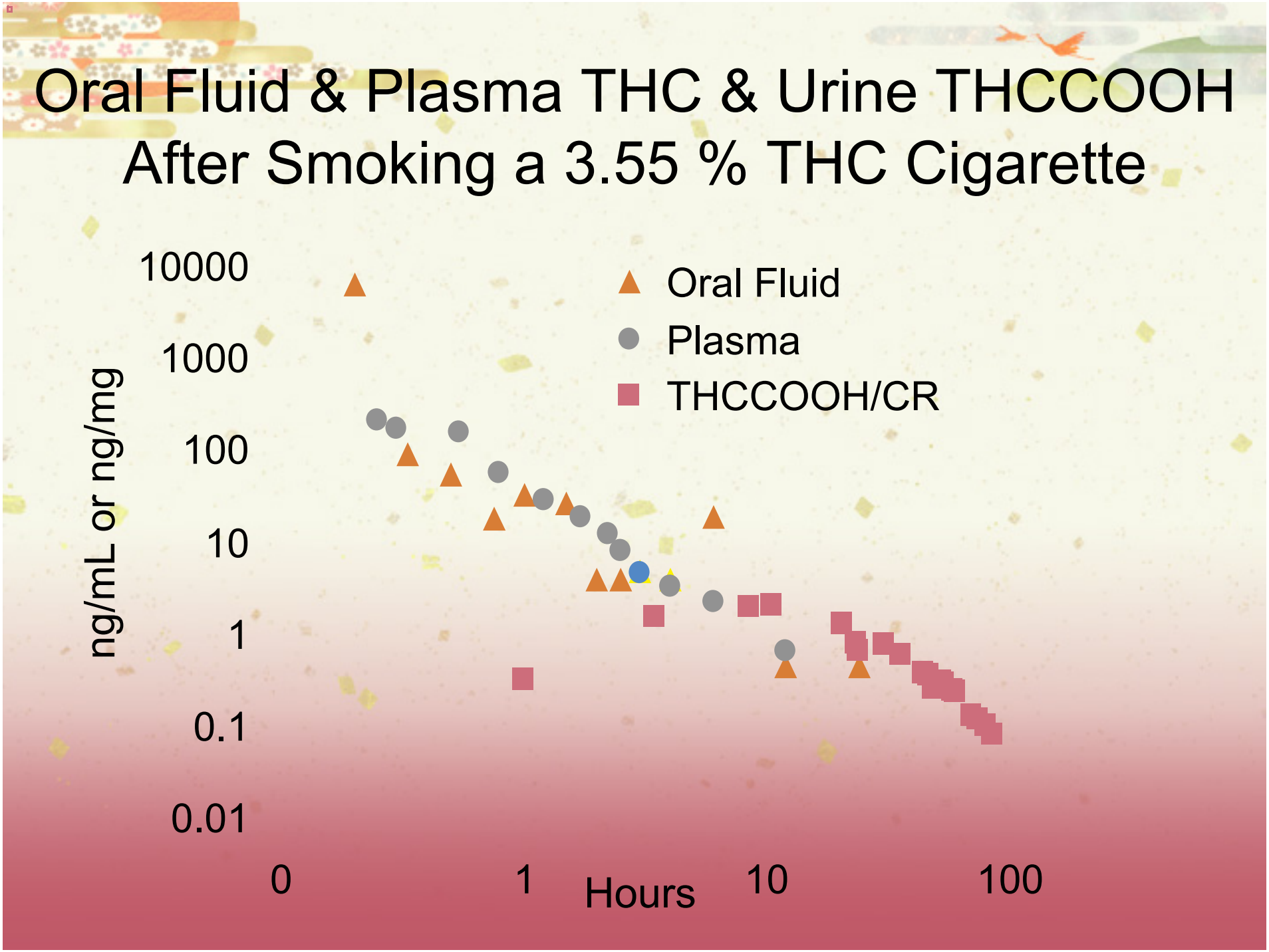
Controlled Codeine Administration



Opiates

- Presley et al FSI 2003
  - Tested 77,218 workplace oral fluid specimens
  - 66.7% of opiate positive tests positive for 6AM
  - 6AM stabilized in acidic pH oral fluid
  - Mean morphine 755 ± 201 ng/mL, 6AM 416 ± 148 ng/mL, codeine 196 ± 36 ng/mL
- Finding heroin, 6AM, &/or acetylcodeine identifies heroin usage
- Rohrig & Moore JAT 2003
  - Eating poppy seeds & morphine-containing foodstuffs produced positive oral fluid morphine at 40 ng/mL for ~ 1 h

Oral Fluid & Plasma THC & Urine THCCOOH After Smoking a 3.55 % THC Cigarette



Oral Fluid Testing

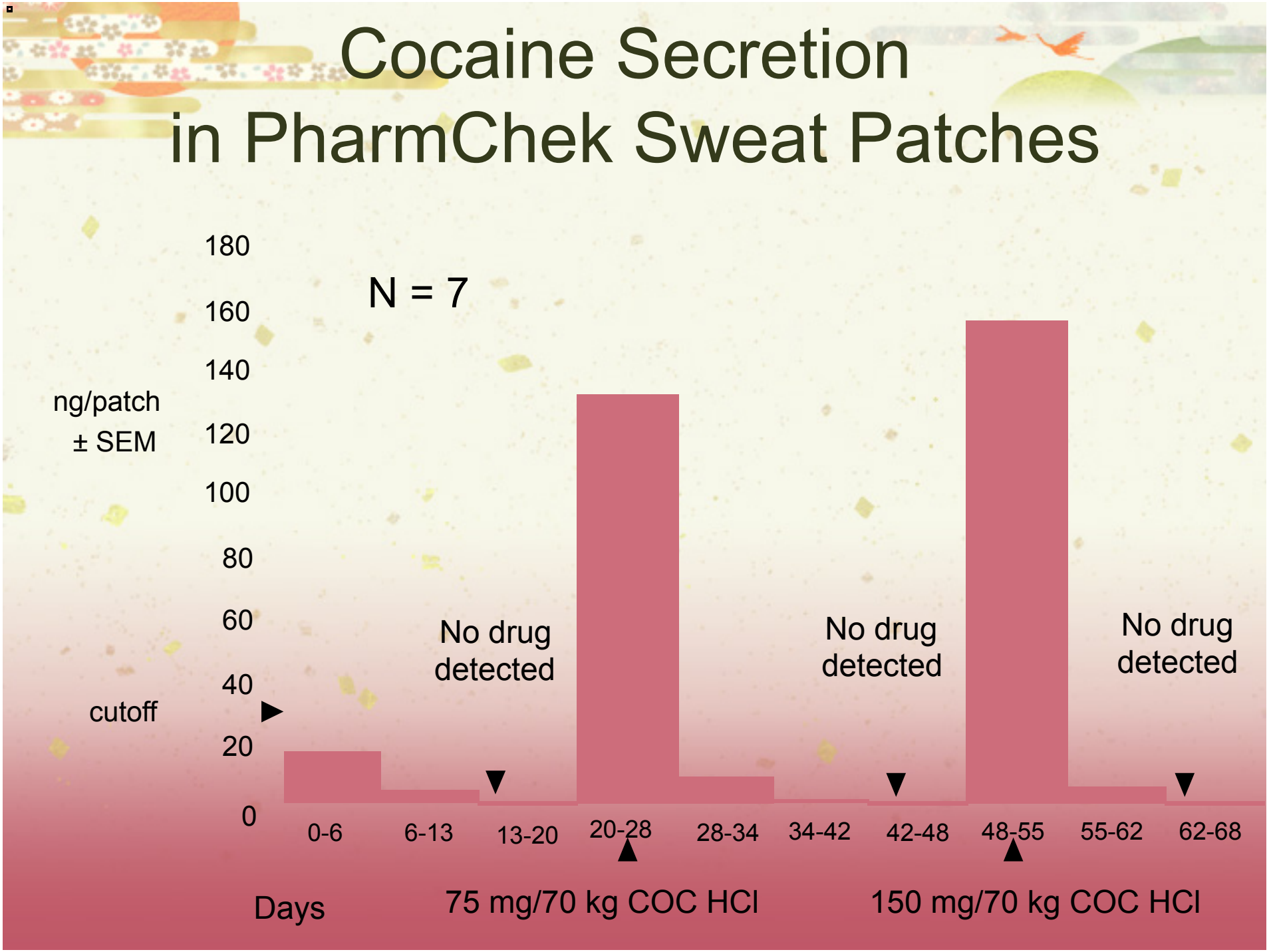
- Strengths:
  - Observed, non-invasive collection
  - More difficult to adulterate
  - Gender neutral specimen collection
  - Basic drugs concentrate in lower pH of oral fluid as compared to blood
  - May correlate with plasma concentrations
  - Reflects more recent drug use (cutoff dependent)
  - On-site technology being developed

Oral Fluid Testing

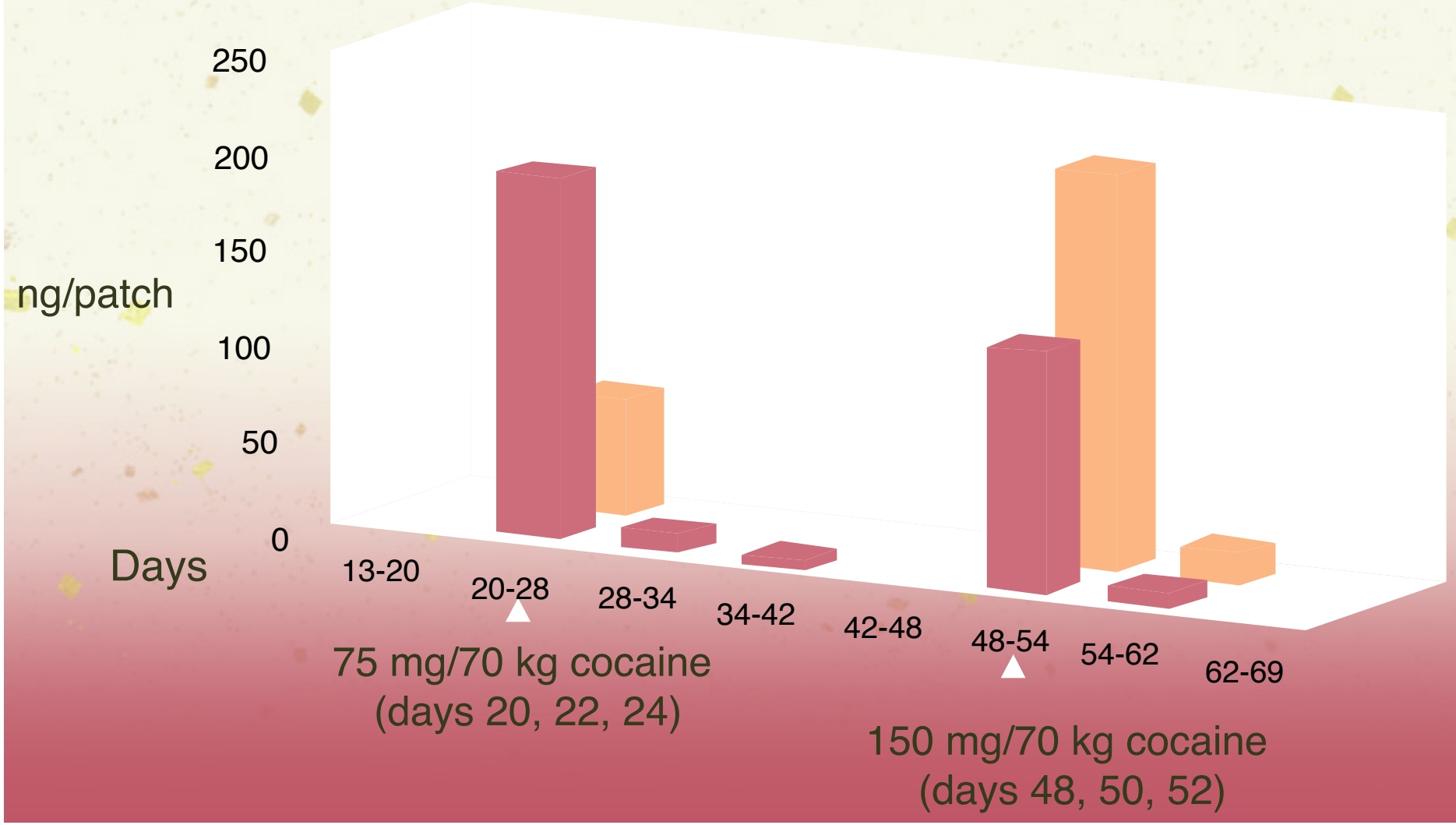
- Limitations:
  - Specimen volume
    - Generally low, especially after stimulant use
    - Many devices have Unknown volume collected
  - Drug adsorption to collection device
  - Elution buffer
    - Differential drug recovery
    - Dilutes oral fluid reducing sensitivity
    - May interfere with LCMS techniques
  - Potential for passive contamination from smoked & oral drugs


Sweat Testing

Cocaine Secretion in PharmChek Sweat Patches

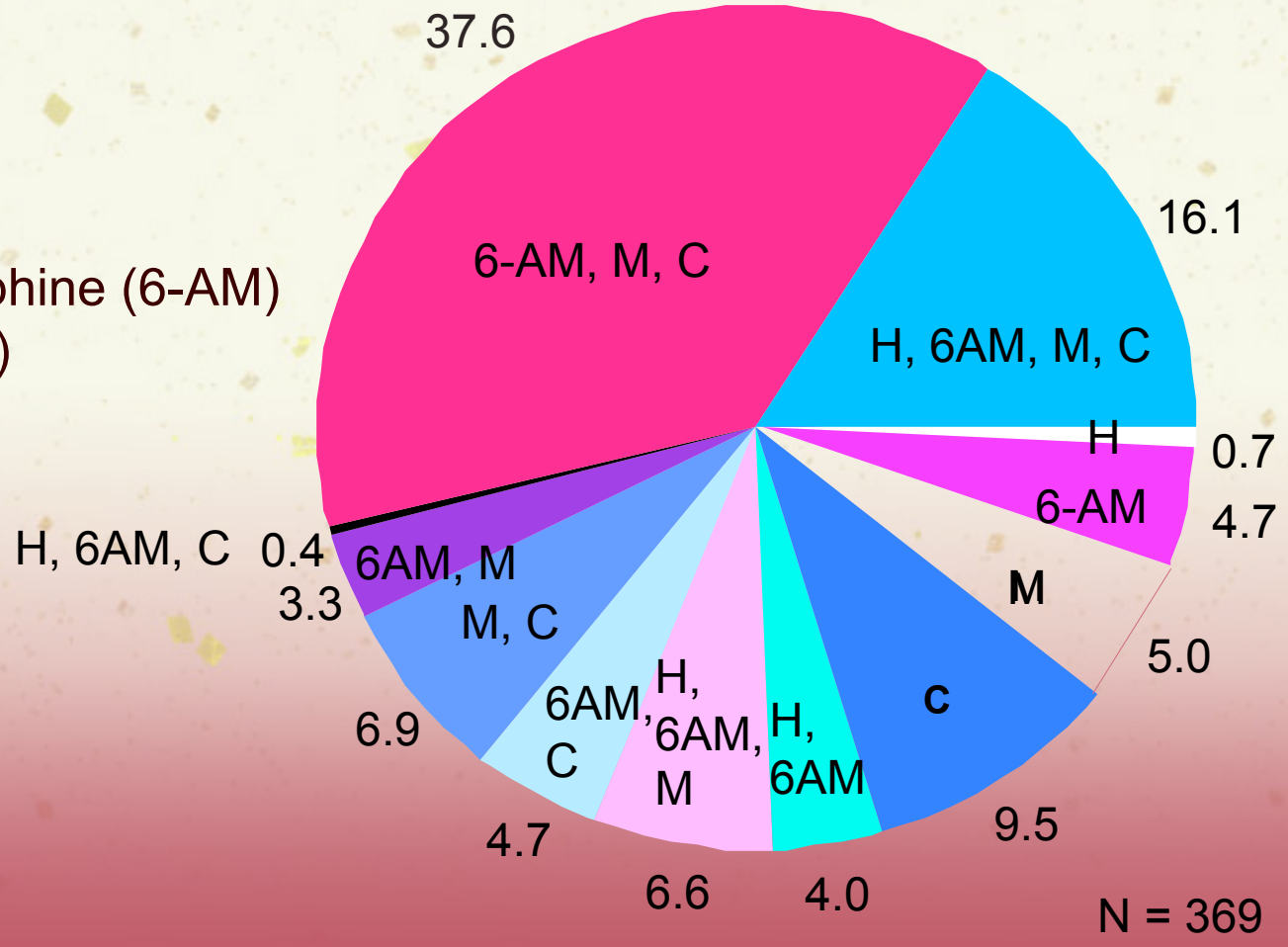


Variable Cocaine Concentrations in Sweat



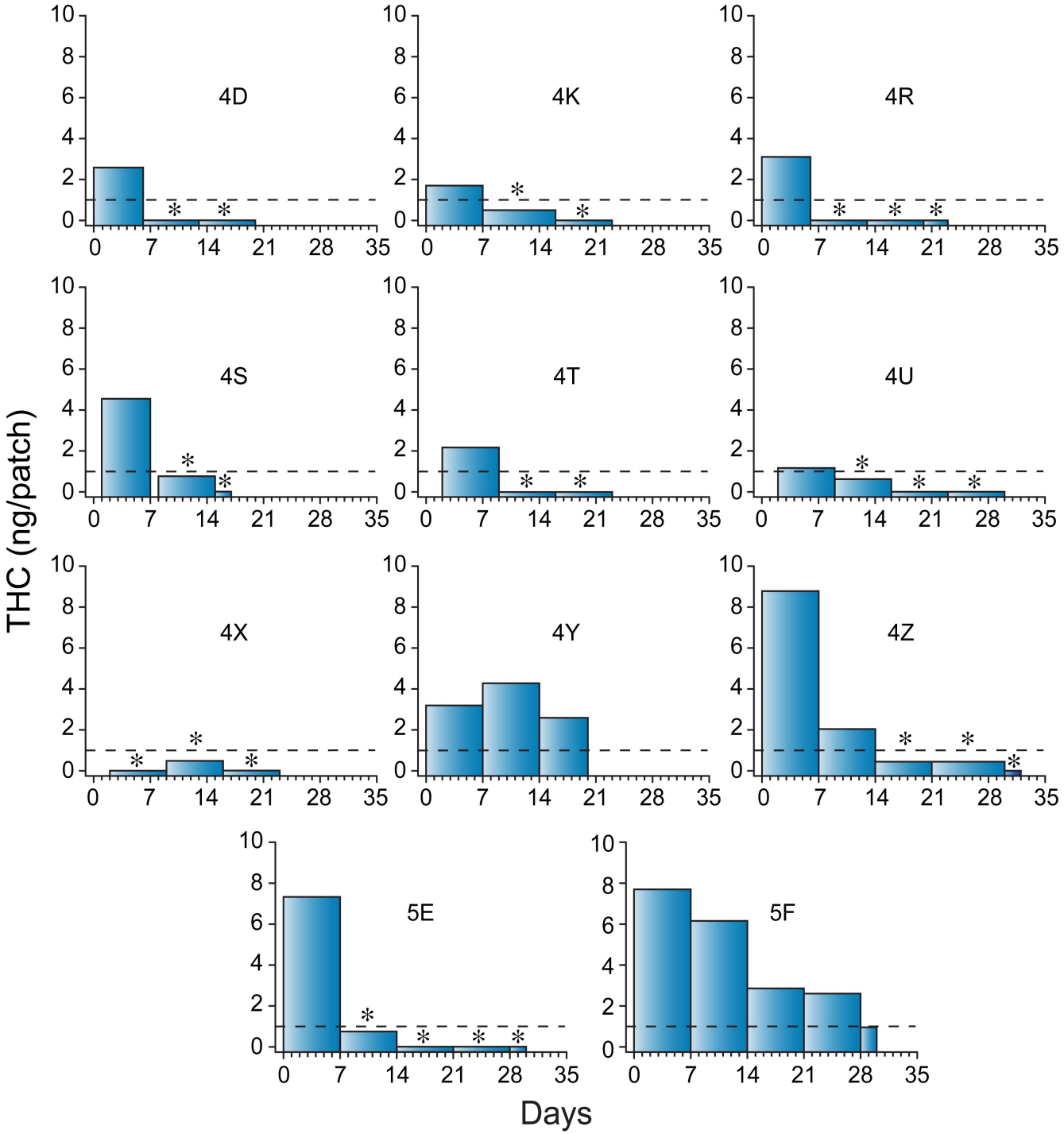
78% Opiate Positive Sweat Patches After Heroin Self-Administration Positive for Heroin &/or 6-AM

Heroin (H)
6-Acetylmorphine (6-AM)
Morphine (M)
Codeine (C)



Cannabinoids in Sweat

- Sweat
  - THC present at low ng/patch concentrations
  - Extraction efficiency low from patch
  - Unknown drug reabsorption through skin
  - Almost no controlled drug administration data
    - After oral 14.8 mg THC per day for 5 days, no positive sweat patches



THC sweat excretion in 11 heavy cannabis users during abstinence with 24 h monitoring

Dashed line indicates 1.0 ng/patch cutoff proposed by SAMHSA

* Negative sweat patch at LOQ of 0.4 ng/patch.

Sweat Testing

- Advantages
  - Convenient & less invasive method for monitoring drug use
  - Window of detection ≥ urine testing (dependent upon drug class)
  - Cumulative measure of exposure
  - Presence of parent drug (heroin, 6AM)
  - Difficult to adulterate specimen

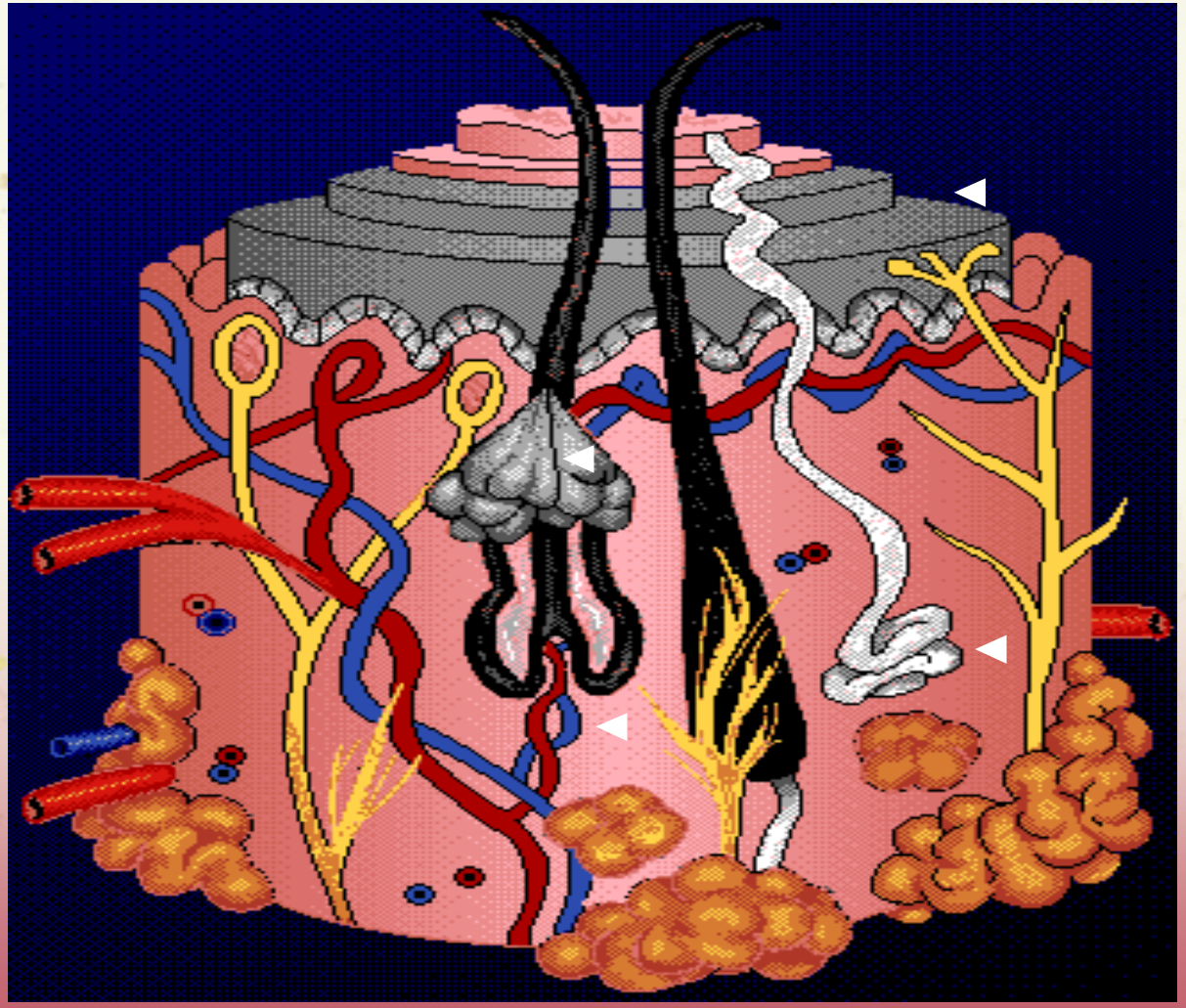
Sweat Testing

- Disadvantages
  - Variation in sweat production
  - Low analyte concentrations
  - Occasional skin sensitivity
  - Dose-response relationships?
  - Residual excretion of drug?
  - Contamination during handling?

Hair

Multiple Sources of Drugs in Hair

External contamination



Skin

Sebum

Sweat
Blood

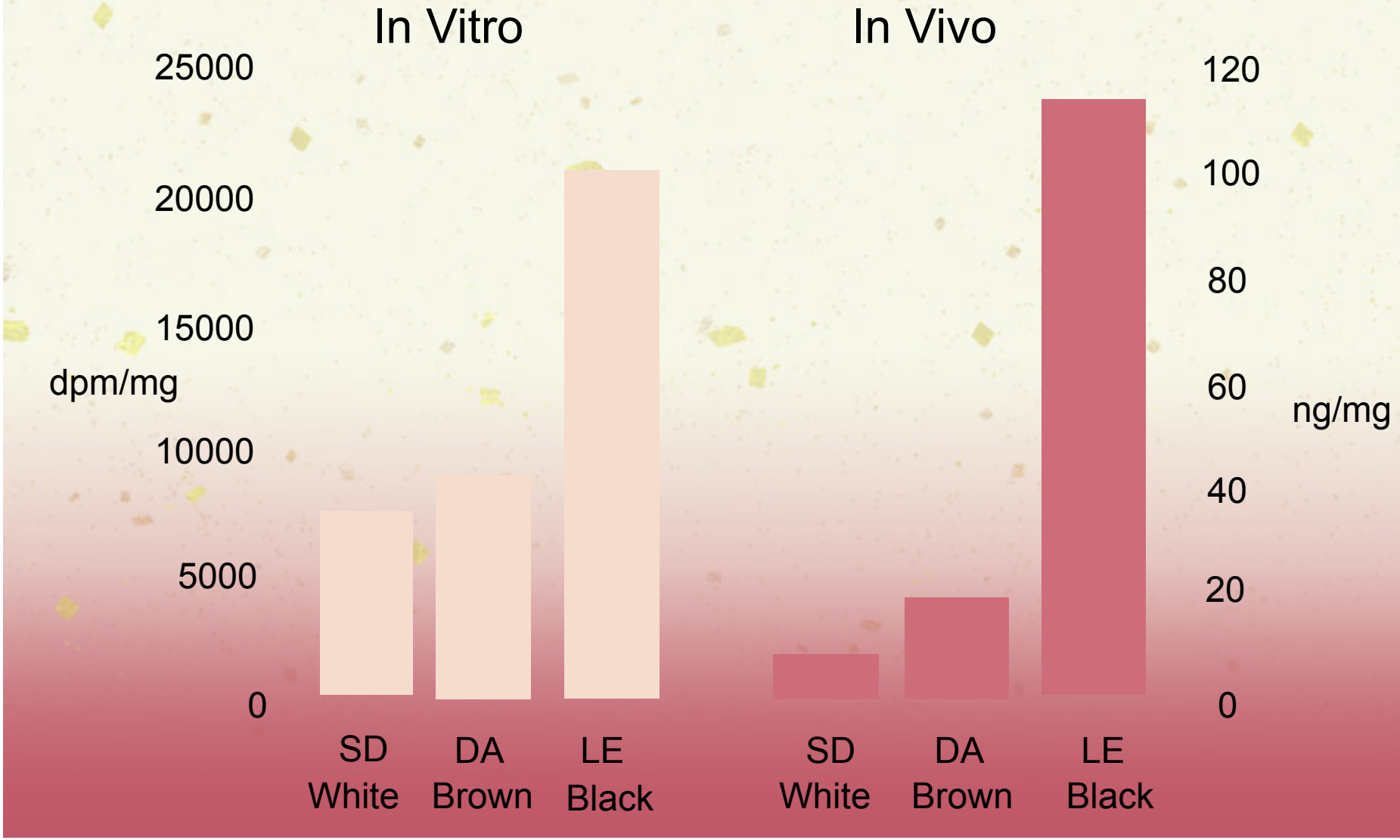
Unanswered Questions

- Color bias: melanin content affects drug deposition?
- Dose-concentration relationships?
- Minimum dose for drug detection?
- Are externally applied drugs removed by washing?
- Does segmental analysis reflect drug use history?
- Are there specific biomarkers that eliminate concern about external contamination of hair?
  - Cocaethylene, norcocaine, benzoylecgonine (BE), BE/cocaine ratio
  - Recent evidence that these biomarkers present in both US Pharmacopeia & street cocaine

D5Cocaine Time Course in Human Hair

Courtesy: Henderson & Harkey, "Hair Analysis of Drugs of Abuse", Final Report, 1993

In Vitro vs In Vivo
Codeine Incorporation Into Rat Hair



Cannabinoids in Hair

- Non-daily cannabis users (N = 33)
  (1 - 5 joints or blunts per week)
  - 30% cannabinoid screen pos ≥ 5 pg/mg
  - 72.7% THC ≥ 1 pg/mg
  - 80% THCCOOH ≥ 0.1 pg/mg
- Daily cannabis users (N = 20)
  - 65% cannabinoid screen pos ≥ 5 pg/mg
  - 60% THC ≥ 1 pg/mg
  - 80% THCCOOH ≥ 0.1 pg/mg

Cannabinoids in Hair

- Hair
  - Least sensitive matrix for cannabis detection
  - Almost no controlled drug administration data
  - Potential for contamination from cannabis smoke requires measurement of THCCOOH by tandem mass spectrometry

Advantages of Hair Testing

- Large window of drug detection
- Brief periods of abstinence will not alter test outcome
- Hair is easy to collect, handle & store
- Collection less invasive than urine collection
- Retesting can be accomplished
- Adulteration of hair test may be more difficult or more apparent

Disadvantages of Hair Testing

- Hair melanin concentration affects drug incorporation of basic drugs (color bias?)
- Poor incorporation of neutral & acidic drugs: low concentrations (pg/mg)
- Possibility of environmental contamination from smoked drugs
- Recent drug use not detected
- Expensive, frequently requires tandem mass spectrometry, highly trained analysts
- Few controlled studies to guide interpretation

Quest Diagnostics Drug Testing Index Data To Be Released After August 20 Represent >500,000 tests in 2009

% Positive Opiates Workplace Testing Pre-employment

	2005	2006	2007	2008	2009
COD	0.22	0.19	0.16	0.19	0.18
MOR	0.34	0.30	0.29	0.31	0.32
HC	0.69	0.70	0.79	0.78	0.78
HM	0.37	0.38	0.48	0.50	0.47
OXYC	0.56	0.64	0.88	0.83	1.00

% Positive Opiates Post-accident Positivity Rates

	2005	2006	2007	2008	2009
COD	0.36	0.31	0.30	0.34	0.46
MOR	1.0	0.90	1.0	1.2	1.2
HC	2.3	2.1	2.9	3.2	3.7
HM	1.2	1.2	1.8	2.2	2.3

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